SEQUENCE LISTING

```
FEB 2 2 2001 STATE OF THE PADEMARK CHE
```

```
<110> Max-Delbrück-Centrum für Molekulare Medizin
```

<120> Novel Sequence Variants of the Human Beta 2-Adrenergic Redeptor Gene and Use Thereof

```
<130> Ref.\ 101195-2
```

RECEIVED

<140> Ser. No. 09/582,719

MAR 0 1 2001

<141> 2000-06-29

TECH CENTER 1600/2900

<150> DE 197 58 401.2

<151> 1997-12 \ 30

<150> PCT/DE98/03818

<151> 1998-12-30

<160> 7

<170> PatentIn Ven. 2.1

<210> 1

<211> 3451

<212> DNA

<213> human genomic dlone

<220>

<221> mutation

<222> (1)..(3451)

<223> variant of the human beta2-adrenergic receptor
 gene with mutations in positions
 159,245,565,934,1120,1221,1541,1568,1633,1666,1839
 ,2078,2110,2640,2826

<400> 1

cccgggttca agagattctc ctgtctcage ctcccgagta gctgggacta caggtacgtg 60 ccaccacacc tggctaattt ttgtatttt agtagagaca agagttacac catattggcc 120 aggatctttt gctttctata gcttcaaaat gttcttaaag ttaagacatt cttaatactc 180 tgaaccatat gaatttgcca ttttggtaag tcacagacge cagatggtgg caatttcaca 240 tggggcaacc cgaaagatta acaaactatc cagcagatga aaggatttt tttagtttca 300 ttgggtttac tgaagaaatt gtttgaattc tcattgcatc tccagttcaa cagataatga 360 gtgagtgatg ccacactctc aagagttaaa aacaaacaa caaaaaaatt aaaacaaaag 420 cacacacactt tctctctctg tcccaaaata catacttgca tacccccgct ccagataaaa 480 tccaaagggt aaaactgtct tcatgcctg aaattcctaa ggagggcacc taaagtactt 540 gacagcgagt gtgctgagga aatcagcagc tgttgaagtc acctcctgtg ctcttgccaa 600 gctcgggtga ggcaagttcg gagtacccag atggagacat ccgtgtctgt gtcgctctgg 720

atgcctccaa gccagcgtgt gtttactttc tgtgtgtgtc accatgtctt tgtgcttctg 780 ggtgcttctg tgtttgtttc tggccgcgtt tctgtgttgg acaggggtga ctttgtgccg 840 gatggettet gtgtgagage gegegegagt gtgcatgteg gtgagetggg agggtgtgte 900 tcagtgtcta tggctgtggt tcggtataag tctaagcatg tctgccaggg tgtatttgtg 960 cctgtatgtg cgtgcctcgg tgggcactct cgtttccttc cgaatgtggg gcagtgccgg 1020 tgtgctgccc tctgccttga gacctcaagc cgcgcaggcg cccagggcag gcaggtagcg 1080 gccacagaag agccaaaagc tcccgggttg gctggtaagc acaccacctc cagctttagc 1140 cctctqqqqc caqccagggt agccgggaag cagtggtggc ccgcctcca gggagcagtt 1200 gagtgcctcg ccccttcgcg gctgccggcg tgccattggc cgaaagttcc cgtacgtcac 1320 ggcgagggca gttcccctaa agtcctgtgc acataacggg cagaacgcac tgcgaagcgg 1380 cttcttcaga gcacgggctg gaactggcag gcaccgcgag cccctagcac ccgacaagct 1440 gagtgtgcag gacgagtccc caccacaccc acaccacagc cgctgaatga ggcttccagg 1500 cgtccgctcg cggcccgcag agecccgccg tgggtccgcc tgctgaggcg cccccagcca 1560 gtgcgctcac ctgccagact gcgcgccatg gggcaacccg ggaacggcag cgccttcttg 1620 ctggcaccca atggaagcca tgcgccggac cacgacgtca cgcaggaaag ggacgaggtg 1680 tgggtggtgg gcatgggcat cgtcatgtct ctcatcgtcc tggccatcgt gtttggcaat 1740 gtgctggtca tcacagccat tgccaagttc gagcgtctgc agacggtcac caactacttc 1800 atcacttcac tggcctgtgc tgatctggtc atgggcctag cagtggtgcc ctttggggcc 1860 gcccatattc ttatgaaaat gtggactttt ggcaacttct ggtgcgagtt ttggacttcc 1920 attgatgtgc tgtgcgtcac ggccagcatt gagaccctgt gcgtgatcgc agtggatcgc 1980 tactttgcca ttacttcacc tttcaagtac cagagcctgc tgaccaagaa taaggcccgg 2040 gtgatcattc tgatggtgtg gattgtgtca ggccttatct ccttcttgcc cattcagatg 2100 cactggtaca gggccaccca ccaggaagcc atcaactgct atgccaatga gacctgctgt 2160 gacttettea egaaceaage etatgeeatt geetetteea tegtgteett etaegtteee 2220 ctggtgatca tggtcttcgt ctactccagg gtctttcagg aggccaaaag gcagctccag 2280 aagattgaca aatctgaggg ccgcttccat gtccagaacc ttagccaggt ggagcaggat 2340 gggcggacgg ggcatggact ccgcagatct tccaagttct gcttgaagga gcacaaagcc 2400 ctcaagacgt taggcatcat catgggcact ttcaccctct gctggctgcc cttcttcatc 2460 gttaacattg tgcatgtgat ccaggataac ctcatccgta aggaagttta catcctccta 2520 aattggatag gctatgtcaa ttctggtttc aatcccctta tctactgccg gagcccagat 2580 ttcaggattg ccttccagga gcttctgtgc ctgcgcaggt cttctttgaa ggcctatggc 2640 aatggctact ccagcaacgg caacacaggg gagcagagtg gatatcacgt ggaacaggag 2700 aaagaaaata aactgctgtg tgaagacctc ccaggcacgg aagactttgt gggccatcaa 2760 qqtactgtqc ctagcgataa cattgattca caagggagga attgtagtac aaatgactca 2820 ctgctataaa gcagtttttc tacttttaaa gaccccccc cccccaacag aacactaaac 2880 agactattta acttgagggt aataaactta gaataaaatt gtaaaaattg tatagagata 2940 tgcagaagga agggcatcct tctgcctttt ttattttttt aagctgtaaa aagagagaaa 3000 aagtttatgt ctaaagagct ttagtcctag aggacctgag tctgctatat tttcatgact 3120 tttccatgta tctacctcac tattcaagta ttaggggtaa tatattgctg ctggtaattt 3180 gtatctgaag gagattttcc ttcctacacc cttggacttg aggattttga gtatctcgga 3240 cettteaget gtgaacatgg actetteece cacteetett atttgeteac acggggtatt 3300 ttaggcaggg atttgaggag cagcttcagt tgttttcccg agcaaaggtc taaagtttac 3360 agtaaataaa atgtttgacc atgccttcat tgcacctgtt tgtccaaaac cccttgactg 3420 3451 gagtgctgtt gcctcccca ctggaaaccg c

<210> 2
<211> 3451
<212> DNA
<213> human genomic clone

<220>
<221> mutation
<222> (1)..(3451)
<223> variant of the human beta2-adrenergic receptor gene with mutations in positions 1541,1633,1666

<400> 2 cccgggttca agagattctc ctgtctcagc ctcccgagta gctgggacta caggtacgtg 60 ccaccacacc tggctaattt ttgtattttt agtagagaca agagttacac catattggcc 120 aggatetttt getttetata getteaaaat gttettaatg ttaagaeatt ettaataete 180 tgaaccatat gaatttgcca ttttggtaag tcacagacgc cagatggtgg caatttcaca 240 tggcacaacc cgaaagatta acaaactatc cagcagatga aaggattttt tttagtttca 300 ttgggtttac tgaagaaatt gtttgaattc tcattgcatc tccagttcaa cagataatga 360 cacacaactt tetetetetg teccaaaata cataettgea taceeegget eeagataaaa 480 tccaaagggt aaaactgtct tcatgcctgc aaattcctaa ggagggcacc taaagtactt 540 gacagegagt gtgctgagga aateggeage tgttgaagte aceteetgtg etettgeeaa 600 gctcgggtga ggcaagttcg gagtacccag atggagacat ccgtgtctgt gtcgctctgg 720 atgcctccaa gccagcgtgt gtttactttc tgtgtgtgtc accatgtctt tgtgcttctg 780 ggtgettetg tgtttgttte tggeegegtt tetgtgttgg acaggggtga etttgtgeeg 840 gatggettet gtgtgagage gegegegagt gtgcatgteg gtgagetggg agggtgtgte 900 tcagtgtcta tggctgtggt tcggtataag tctgagcatg tctgccaggg tgtatttgtg 960 cctgtatgtg cgtgcctcgg tgggcactct cgtttccttc cgaatgtggg gcagtgccgg 1020 tgtgctgccc tctgccttga gacctcaagc cgcgcaggcg cccagggcag gcaggtagcg 1080 gccacagaag agccaaaagc tcccgggttg gctggtaagg acaccacctc cagctttagc 1140 cctctggggc cagccagggt agccgggaag cagtggtggc ccgccctcca gggagcagtt 1200 gggccccgcc cgggccagcc ccaggagaag gagggcgagg ggaggggagg gaaaggggag 1260 gagtgcctcg ccccttcgcg gctgccggcg tgccattggc cgaaagttcc cgtacgtcac 1320 ggcgagggca gttcccctaa agtcctgtgc acataacggg cagaacgcac tgcgaagcgg 1380 cttcttcaga gcacgggctg gaactggcag gcaccgcgag cccctagcac ccgacaagct 1440 gagtgtgcag gacgagtccc caccacacc acaccacagc cgctgaatga ggcttccagg 1500 cgtccgctcg cggcccgcag agccccgccg tgggtccgcc tgctgaggcg cccccagcca 1560 gtgcgcttac ctgccagact gcgcgccatg gggcaacccg ggaacggcag cgccttcttg 1620 ctggcaccca atagaagcca tgcgccggac cacgacgtca cgcagcaaag ggacgaggtg 1680 tgggtggtgg gcatgggcat cgtcatgtct ctcatcgtcc tggccatcgt gtttggcaat 1740 gtgctggtca tcacagccat tgccaagttc gagcgtctgc agacggtcac caactacttc 1800 atcacttcac tggcctgtgc tgatctggtc atgggcctgg cagtggtgcc ctttggggcc 1860 gcccatattc ttatgaaaat gtggactttt ggcaacttct ggtgcgagtt ttggacttcc 1920 attgatgtgc tgtgcgtcac ggccagcatt gagaccctgt gcgtgatcgc agtggatcgc 1980 tactttgcca ttacttcacc tttcaagtac cagagcctgc tgaccaagaa taaggcccgg 2040 gtgatcattc tgatggtgtg gattgtgtca ggccttacct ccttcttgcc cattcagatg 2100 cactggtacc gggccaccca ccaggaagcc atcaactgct atgccaatga gacctgctgt 2160

gacttettea egaaceaage etatgeeatt geetetteea tegtgteett etaegtteee 2220 ctggtgatca tggtcttcgt ctactccagg gtctttcagg aggccaaaag gcagctccag 2280 aagattgaca aatctgaggg ccgcttccat gtccagaacc ttagccaggt ggagcaggat 2340 gggcggacgg ggcatggact ccgcagatct tccaagttct gcttgaagga gcacaaagcc 2400 ctcaagacgt taggcatcat catgggcact ttcaccctct gctggctgcc cttcttcatc 2460 gttaacattg tgcatgtgat ccaggataac ctcatccgta aggaagttta catcctccta 2520 aattggatag gctatgtcaa ttctggtttc aatcccctta tctactgccg gagcccagat 2580 ttcaggattg ccttccagga gcttctgtgc ctgcgcaggt cttctttgaa ggcctatggg 2640 aatggctact ccagcaacgg caacacaggg gagcagagtg gatatcacgt ggaacaggag 2700 aaagaaaata aactgctgtg tgaagacctc ccaggcacgg aagactttgt gggccatcaa 2760 ggtactgtgc ctagcgataa cattgattca caagggagga attgtagtac aaatgactca 2820 ctgctgtaaa gcagtttttc tacttttaaa gaccccccc cccccaacag aacactaaac 2880 agactattta acttgagggt aataaactta gaataaaatt gtaaaaattg tatagagata 2940 tgcagaagga agggcatcct tctgcctttt ttattttttt aagctgtaaa aagagagaaa 3000 aagtttatgt ctaaagagct ttagtcctag aggacctgag tctgctatat tttcatgact 3120 tttccatgta tctacctcac tattcaagta ttaggggtaa tatattgctg ctggtaattt 3180 gtatctgaag gagattttcc ttcctacacc cttggacttg aggattttga gtatctcgga 3240 cettteaget gtgaacatgg actetteece cacteetett atttgeteac acggggtatt 3300 ttaggcaggg atttgaggag cagcttcagt tgttttcccg agcaaaggtc taaagtttac 3360 agtaaataaa atgtttgacc atgccttcat tgcacctgtt tgtccaaaac cccttgactg 3420 gagtgctgtt gcctccccca ctggaaaccg c

```
<210> 3
<211> 3451
<212> DNA
<213> human genomic clone

<220>
<221> mutation
<222> (1)..(3451)
<223> variant of the human beta2-adrenergic receptor gene with mutations in positions 1541,1633,1666
```

cccgggttca agagattctc ctgtctcagc ctcccgagta gctgggacta caggtacgtg 60 ccaccacacc tggctaattt ttgtattttt agtagagaca agagttacac catattggcc 120 aggatctttt gctttctata gcttcaaaat gttcttaatg ttaagacatt cttaatactc 180 tgaaccatat gaatttgcca ttttggtaag tcacagacgc cagatggtgg caatttcaca 240 tggcacaacc cgaaagatta acaaactatc cagcagatga aaggattttt tttagtttca 300 ttgggtttac tgaagaaatt gtttgaattc tcattgcatc tccagttcaa cagataatga 360 gtgagtgatg ccacactctc aagagttaaa aacaaacaa caaaaaaatt aaaacaaaag 420 cacacactt tctctctg tcccaaaata catacttgca tacccccgct ccagataaaa 480 tccaaagggt aaaactgtct tcatgcctgc aaattcctaa ggagggcacc taaagtactt 540 gacagcgagt gtgctgagga aatcggcagc tgttgaagtc acctcctgtg ctcttgccaa 600 gctcgggtga ggcaagttcg gagtacccag atggagacac ccgtgtctgt gtcgctctgg 720

atgectecaa gecagegtgt gtttacttte tgtgtgtgte accatgtett tgtgettetg 780 qqtqcttctg tgtttgtttc tggccgcgtt tctgtgttgg acaggggtga ctttgtgccg 840 gatggcttct gtgtgagagc gcgcgcgagt gtgcatgtcg gtgagctggg agggtgtgtc 900 tcagtgtcta tggctgtggt tcggtataag tctgagcatg tctgccaggg tgtatttgtg 960 cctgtatgtg cgtgcctcgg tgggcactct cgtttccttc cgaatgtggg gcagtgccgg 1020 tgtgctgccc tctgccttga gacctcaagc cgcgcaggcg cccagggcag gcaggtagcg 1080 gccacagaag agccaaaagc tcccgggttg gctggtaagg acaccacctc cagctttagc 1140 cctctggggc cagccagggt agccgggaag cagtggtggc ccgccctcca gggagcagtt 1200 gggccccgcc cgggccagcc ccaggagaag gagggcgagg ggaggggagg gaaaggggag 1260 gagtgcctcg ccccttcgcg gctgccggcg tgccattggc cgaaagttcc cgtacgtcac 1320 ggcgagggca gttcccctaa agtcctgtgc acataacggg cagaacgcac tgcgaagcgg 1380 cttcttcaga gcacgggctg gaactggcag gcaccgcgag cccctagcac ccgacaagct 1440 gagtgtgcag gacgagtccc caccacaccc acaccacagc cgctgaatga ggcttccagg 1500 cgtccgctcg cggcccgcag agccccgccg tgggtccgcc cgctgaggcg cccccagcca 1560 gtgcgcttac ctgccagact gcgcgccatg gggcaacccg ggaacggcag cgccttcttg 1620 ctggcaccca atggaagcca tgcgccggac cacgacgtca cgcaggaaag ggacgaggtg 1680 tgggtggtgg gcatgggcat cgtcatgtct ctcatcgtcc tggccatcgt gtttggcaat 1740 qtqctqqtca tcacaqccat tqccaaqttc gagcqtctqc agacqqtcac caactacttc 1800 atcacttcac tggcctgtgc tgatctggtc atgggcctgg cagtggtgcc ctttggggcc 1860 gcccatattc ttatgaaaat gtggactttt ggcaacttct ggtgcgagtt ttggacttcc 1920 attgatgtgc tgtgcgtcac ggccagcatt gagaccctgt gcgtgatcgc agtggatcgc 1980 tactttgcca ttacttcacc tttcaagtac cagagcctgc tgaccaagaa taaggcccgg 2040 gtgatcattc tgatggtgtg gattgtgtca ggccttacct ccttcttgcc cattcagatg 2100 cactggtacc gggccaccca ccaggaagcc atcaactgct atgccaatga gacctgctgt 2160 gacttettea egaaceaage etatgeeatt geetetteea tegtgteett etaegtteee 2220 ctggtgatca tggtcttcgt ctactccagg gtctttcagg aggccaaaag gcagctccag 2280 aagattgaca aatctgaggg ccgcttccat gtccagaacc ttagccaggt ggagcaggat 2340 gggcggacgg ggcatggact ccgcagatct tccaagttct gcttgaagga gcacaaagcc 2400 ctcaagacgt taggcatcat catgggcact ttcaccctct gctggctgcc cttcttcatc 2460 gttaacattg tgcatgtgat ccaggataac ctcatccgta aggaagttta catcctccta 2520 aattggatag gctatgtcaa ttctggtttc aatcccctta tctactgccg gagcccagat 2580 ttcaggattg ccttccagga gcttctgtgc ctgcgcaggt cttctttgaa ggcctatggg 2640 aatggctact ccagcaacgg caacacaggg gagcagagtg gatatcacgt ggaacaggag 2700 aaagaaaata aactgctgtg tgaagacctc ccaggcacgg aagactttgt gggccatcaa 2760 ggtactgtgc ctagcgataa cattgattca caagggagga attgtagtac aaatgactca 2820 ctgctgtaaa gcagtttttc tacttttaaa gaccccccc cccccaacag aacactaaac 2880 agactattta acttgagggt aataaactta gaataaaatt gtaaaaattg tatagagata 2940 tgcagaagga agggcatcct tctgcctttt ttattttttt aagctgtaaa aagagagaaa 3000 aagtttatgt ctaaagagct ttagtcctag aggacctgag tctgctatat tttcatgact 3120 tttccatgta tctacctcac tattcaagta ttaggggtaa tatattgctg ctggtaattt 3180 gtatctgaag gagattttcc ttcctacacc cttggacttg aggattttga gtatctcgga 3240 cctttcagct gtgaacatgg actcttcccc cactcctctt atttgctcac acggggtatt 3300 ttaggcaggg atttgaggag cagcttcagt tgttttcccg agcaaaggtc taaagtttac 3360 agtaaataaa atgtttgacc atgccttcat tgcacctgtt tgtccaaaac cccttgactg 3420 3451 gagtgctgtt gcctccccca ctggaaaccg c

<210> 4
<211> 3451
<212> DNA
<213> human genomic clone

<220>
<221> mutation
<222> (1)..(3451)
<223> variant of the human beta2-adernergic receptor gene with mutations in positions 1541,1633,1666

<400> 4 cccgggttca agagattctc ctgtctcagc ctcccgagta gctgggacta caggtacgtg 60 ccaccacacc tggctaattt ttgtattttt agtagagaca agagttacac catattggcc 120 aggatetttt getttetata getteaaaat gttettaatg ttaagaeatt ettaataete 180 tgaaccatat gaatttgcca ttttggtaag tcacagacgc cagatggtgg caatttcaca 240 tggcacaacc cgaaagatta acaaactatc cagcagatga aaggattttt tttagtttca 300 ttgggtttac tgaagaaatt gtttgaattc tcattgcatc tccagttcaa cagataatga 360 cacacaactt tetetetetg teecaaaata cataettgea taceeegget eeagataaaa 480 tccaaagggt aaaactgtct tcatgcctgc aaattcctaa ggagggcacc taaagtactt 540 gacagegagt gtgetgagga aateggeage tgttgaagte aceteetgtg etettgeeaa 600 gctcgggtga ggcaagttcg gagtacccag atggagacat ccgtgtctgt gtcgctctgg 720 atgectecaa gecagegtgt gtttacttte tgtgtgtgte accatgtett tgtgettetg 780 ggtgcttctg tgtttgtttc tggccgcgtt tctgtgttgg acaggggtga ctttgtgccg 840 gatggettet gtgtgagage gegegegagt gtgcatgteg gtgagetggg agggtgtgte 900 tcagtgtcta tggctgtggt tcggtataag tctgagcatg tctgccaggg tgtatttgtg 960 cctgtatgtg cgtgcctcgg tgggcactct cgtttccttc cgaatgtggg gcagtgccgg 1020 tgtgctgccc tctgccttga gacctcaagc cgcgcaggcg cccagggcag gcaggtagcg 1080 gccacagaag agccaaaagc tcccgggttg gctggtaagg acaccacctc cagctttagc 1140 cctctggggc cagccagggt agccgggaag cagtggtggc ccgcctcca gggagcagtt 1200 gggccccgcc cgggccagcc ccaggagaag gagggcgagg ggaggggagg gaaaggggag 1260 gagtgcctcg ccccttcgcg gctgccggcg tgccattggc cgaaagttcc cgtacgtcac 1320 ggcgagggca gttcccctaa agtcctgtgc acataacggg cagaacgcac tgcgaagcgg 1380 cttcttcaga gcacgggctg gaactggcag gcaccgcgag cccctagcac ccgacaagct 1440 gagtgtgcag gacgagtccc caccacaccc acaccacagc cgctgaatga ggcttccagg 1500 cgtccgctcg cggcccgcag agccccgccg tgggtccgcc tgctgaggcg cccccagcca 1560 gtgcgcttac ctgccagact gcgcgccatg gggcaacccg ggaacggcag cgccttcttg 1620 ctggcaccca atggaagcca tgcgccggac cacgacgtca cgcagcaaag ggacgaggtg 1680 tgggtggtgg gcatgggcat cgtcatgtct ctcatcgtcc tggccatcgt gtttggcaat 1740 gtgctggtca tcacagccat tgccaagttc gagcgtctgc agacggtcac caactacttc 1800 atcacttcac tggcctgtgc tgatctggtc atgggcctgg cagtggtgcc ctttggggcc 1860 gcccatattc ttatgaaaat gtggactttt ggcaacttct ggtgcgagtt ttggacttcc 1920

attgatgtge tgtgcgteac ggccagcatt gagaccetgt gcgtgatcge agtggatcge 1980 tactttgcca ttacttcace tttcaagtac cagagcetge tgaccaagaa taaggccegg 2040 gtgatcatte tgatggtgtg gattgtgtca ggccttacct cettettgce cattcagatg 2100 cactggtace gggccaccca ccaggaagce atcaactget atgccaatga gacctgctgt 2160

gacttettea egaaceaage etatgeeatt geetetteea tegtgteett etaegtteee 2220 ctggtgatca tggtcttcgt ctactccagg gtctttcagg aggccaaaaag gcagctccag 2280 aagattgaca aatctgaggg ccgcttccat gtccagaacc ttagccaggt ggagcaggat 2340 gggcggacgg ggcatggact ccgcagatct tccaagttct gcttgaagga gcacaaagcc 2400 ctcaagacgt taggcatcat catgggcact ttcaccctct gctggctgcc cttcttcatc 2460 gttaacattg tgcatgtgat ccaggataac ctcatccgta aggaagttta catcctccta 2520 aattggatag gctatgtcaa ttctggtttc aatcccctta tctactgccg gagcccagat 2580 ttcaggattg ccttccagga gcttctgtgc ctgcgcaggt cttctttgaa ggcctatggg 2640 aatggctact ccagcaacgg caacacaggg gagcagagtg gatatcacgt ggaacaggag 2700 aaagaaaata aactgctgtg tgaagacctc ccaggcacgg aagactttgt gggccatcaa 2760 ggtactgtgc ctagcgataa cattgattca caagggagga attgtagtac aaatgactca 2820 ctgctgtaaa gcagtttttc tacttttaaa gaccccccc cccccaacag aacactaaac 2880 agactattta acttgagggt aataaactta gaataaaatt gtaaaaattg tatagagata 2940 tgcagaagga agggcatcct tctgcctttt ttattttttt aagctgtaaa aagagagaaa 3000 aagtttatgt ctaaagagct ttagtcctag aggacctgag tctgctatat tttcatgact 3120 tttccatgta tctacctcac tattcaagta ttaggggtaa tatattgctg ctggtaattt 3180 gtatctgaag gagattttcc ttcctacacc cttggacttg aggattttga gtatctcgga 3240 cctttcagct gtgaacatgg actcttcccc cactcctctt atttgctcac acggggtatt 3300 ttaggcaggg atttgaggag cagcttcagt tgttttcccg agcaaaggtc taaagtttac 3360 agtaaataaa atgtttgacc atgccttcat tgcacctgtt tgtccaaaac cccttgactg 3420 gagtgctgtt gcctccccca ctggaaaccg c 3451

```
<210> 5
<211> 3451
<212> DNA
<213> human genomic clone

<220>
<221> mutation
<222> (1)..(3451)
<223> variant of the human beta2-adrenergic receptor gene with mutations in positions
1541,1568,1633,1666
```

gctcgggtga ggcaagttcg gagtacccag atggagacat ccgtgtctgt gtcgctctgg 720 atgectecaa gecagegtgt gtttacttte tgtgtgtgte accatgtett tgtgettetg 780 ggtgcttctg tgtttgtttc tggccgcgtt tctgtgttgg acaggggtga ctttgtgccg 840 gatggcttct gtgtgagagc gcgcgcgagt gtgcatgtcg gtgagctggg agggtgtgtc 900 tcagtgtcta tggctgtggt tcggtataag tctgagcatg tctgccaggg tgtatttgtg 960 cctgtatgtg cgtgcctcgg tgggcactct cgtttccttc cgaatgtggg gcagtgccgg 1020 tgtgctgccc tctgccttga gacctcaagc cgcgcaggcg cccagggcag gcaggtagcg 1080 gccacagaag agccaaaagc tcccgggttg gctggtaagg acaccacctc cagctttagc 1140 cctctggggc cagccagggt agccgggaag cagtggtggc ccgccctcca gggagcagtt 1200 gggccccgcc cgggccagcc ccaggagaag gagggcgagg ggaggggagg gaaaggggag 1260 gagtgcctcg ccccttcgcg gctgccggcg tgccattggc cgaaagttcc cgtacgtcac 1320 ggcgagggca gttcccctaa agtcctgtgc acataacggg cagaacgcac tgcgaagcgg 1380 cttcttcaga gcacgggctg gaactggcag gcaccgcgag cccctagcac ccgacaagct 1440 gagtgtgcag gacgagtccc caccacacc acaccacagc cgctgaatga ggcttccagg 1500 cgtccgctcg cggcccgcag agccccgccg tgggtccgcc tgctgaggcg cccccagcca 1560 gtgcgcttac ctgccagact gcgcgccatg gggcaacccg ggaacggcag cgccttcttg 1620 ctggcaccca atagaagcca tgcgccggac cacgacgtca cgcagcaaag ggacgaggtg 1680 tgggtggtgg gcatgggcat cgtcatgtct ctcatcgtcc tggccatcgt gtttggcaat 1740 gtgctggtca tcacagccat tgccaagttc gagcgtctgc agacggtcac caactacttc 1800 atcacttcac tggcctgtgc tgatctggtc atgggcctgg cagtggtgcc ctttggggcc 1860 gcccatattc ttatgaaaat gtggactttt ggcaacttct ggtgcgagtt ttggacttcc 1920 attgatgtgc tgtgcgtcac ggccagcatt gagaccctgt gcgtgatcgc agtggatcgc 1980 tactttgcca ttacttcacc tttcaagtac cagagcctgc tgaccaagaa taaggcccgg 2040 gtgatcattc tgatggtgtg gattgtgtca ggccttacct ccttcttgcc cattcagatg 2100 cactggtace gggecaceca ceaggaagee ateaactget atgecaatga gacetgetgt 2160 gacttettea egaaceaage etatgeeatt geetetteea tegtgteett etaegtteee 2220 ctggtgatca tggtcttcgt ctactccagg gtctttcagg aggccaaaag gcagctccag 2280 aagattgaca aatctgaggg ccgcttccat gtccagaacc ttagccaggt ggagcaggat 2340 gggcggacgg ggcatggact ccgcagatct tccaagttct gcttgaagga gcacaaagcc 2400 ctcaagacgt taggcatcat catgggcact ttcaccctct gctggctgcc cttcttcatc 2460 gttaacattg tgcatgtgat ccaggataac ctcatccgta aggaagttta catcctccta 2520 aattggatag gctatgtcaa ttctggtttc aatcccctta tctactgccg gagcccagat 2580 ttcaggattg cettecagga gettetgtge etgegeaggt ettetttgaa ggeetatggg 2640 aatggctact ccagcaacgg caacacaggg gagcagagtg gatatcacgt ggaacaggag 2700 aaagaaaata aactgctgtg tgaagacctc ccaggcacgg aagactttgt gggccatcaa 2760 ggtactgtgc ctagcgataa cattgattca caagggagga attgtagtac aaatgactca 2820 ctgctgtaaa gcagtttttc tacttttaaa gacccccccc ccccaacag aacactaaac 2880 agactattta acttgagggt aataaactta gaataaaatt gtaaaaattg tatagagata 2940 tgcagaagga agggcatcct tctgcctttt ttattttttt aagctgtaaa aagagagaaa 3000 aagtttatgt ctaaagagct ttagtcctag aggacctgag tctgctatat tttcatgact 3120 tttccatgta tctacctcac tattcaagta ttaggggtaa tatattgctg ctggtaattt 3180 gtatctgaag gagattttcc ttcctacacc cttggacttg aggattttga gtatctcgga 3240 cettteaget gtgaacatgg actetteece cacteetett atttgeteac acggggtatt 3300 ttaggcaggg atttgaggag cagcttcagt tgttttcccg agcaaaggtc taaagtttac 3360 agtaaataaa atgtttgacc atgccttcat tgcacctgtt tgtccaaaaac cccttgactg 3420 3451 gagtgctgtt gcctccccca ctggaaaccg c

<210> 6
<211> 3451
<212> DNA
<213> human genomic clone

<220>
<221> mutation
<222> (1)..(3451)
<223> variant of the human beta2-adrenergic receptor gene with mutations in positions
1541,1568,1633,1666

<400> 6 cccgggttca agagattctc ctgtctcagc ctcccgagta gctgggacta caggtacgtg 60 ccaccacacc tggctaattt ttgtattttt agtagagaca agagttacac catattggcc 120 aggatetttt getttetata getteaaaat gttettaatg ttaagaeatt ettaataete 180 tgaaccatat gaatttgcca ttttggtaag tcacagacgc cagatggtgg caatttcaca 240 tggcacaacc cgaaagatta acaaactatc cagcagatga aaggattttt tttagtttca 300 ttgggtttac tgaagaaatt gtttgaattc tcattgcatc tccagttcaa cagataatga 360 cacacaactt tetetetetg teccaaaata cataettgea taceeeget eeagataaaa 480 tccaaagggt aaaactgtct tcatgcctgc aaattcctaa ggagggcacc taaagtactt 540 gacagegagt gtgctgagga aateggeage tgttgaagte aceteetgtg etettgeeaa 600 gctcgggtga ggcaagttcg gagtacccag atggagacat ccgtgtctgt gtcgctctgg 720 atgcctccaa gccagcgtgt gtttactttc tgtgtgtgtc accatgtctt tgtgcttctg 780 ggtgcttctg tgtttgtttc tggccgcgtt tctgtgttgg acaggggtga ctttgtgccg 840 gatggcttct gtgtgagagc gcgcgcgagt gtgcatgtcg gtgagctggg agggtgtgtc 900 tcagtgtcta tggctgtggt tcggtataag tctgagcatg tctgccaggg tgtatttgtg 960 cctgtatgtg cgtgcctcgg tgggcactct cgtttccttc cgaatgtggg gcagtgccgg 1020 tgtgctgccc tctgccttga gacctcaagc cgcgcaggcg cccagggcag gcaggtagcg 1080 gccacagaag agccaaaagc tcccgggttg gctggtaagg acaccacctc cagctttagc 1140 cctctggggc cagccagggt agccgggaag cagtggtggc ccgcctcca gggagcagtt 1200 gggccccgcc cgggccagcc ccaggagaag gagggcgagg ggaggggagg gaaaggggag 1260 gagtgcctcg ccccttcgcg gctgccggcg tgccattggc cgaaagttcc cgtacgtcac 1320 ggcgagggca gttcccctaa agtcctgtgc acataacggg cagaacgcac tgcgaagcgg 1380 cttcttcaga gcacgggctg gaactggcag gcaccgcgag cccctagcac ccgacaagct 1440 gagtgtgcag gacgagtccc caccacaccc acaccacagc cgctgaatga ggcttccagg 1500 cgtccgctcg cggcccgcag agccccgccg tgggtccgcc cgctgaggcg cccccagcca 1560 gtgcgctcac ctgccagact gcgcgccatg gggcaacccg ggaacggcag cgccttcttg 1620 ctggcaccca atggaagcca tgcgccggac cacgacgtca cgcaggaaag ggacgaggtg 1680 tgggtggtgg gcatgggcat cgtcatgtct ctcatcgtcc tggccatcgt gtttggcaat 1740 gtgctggtca tcacagccat tgccaagttc gagcgtctgc agacggtcac caactacttc 1800 atcacttcac tggcctgtgc tgatctggtc atgggcctgg cagtggtgcc ctttggggcc 1860 gcccatattc ttatgaaaat gtggactttt ggcaacttct ggtgcgagtt ttggacttcc 1920

attgatgtgc tgtgcgtcac ggccagcatt gagaccctgt gcgtgatcgc agtggatcgc 1980 tactttgcca ttacttcacc tttcaagtac cagagcctgc tgaccaagaa taaggcccgg 2040

gtgatcattc tgatggtgtg gattgtgtca ggccttacct ccttcttgcc cattcagatg 2100 cactggtacc gggccaccca ccaggaagcc atcaactgct atgccaatga gacctgctgt 2160 gacttettea egaaceaage etatgeeatt geetetteea tegtgteett etaegtteee 2220 ctggtgatca tggtcttcgt ctactccagg gtctttcagg aggccaaaag gcagctccag 2280 aagattgaca aatctgaggg ccgcttccat gtccagaacc ttagccaggt ggagcaggat 2340 gggcggacgg ggcatggact ccgcagatct tccaagttct gcttgaagga gcacaaagcc 2400 ctcaagacgt taggcatcat catgggcact ttcaccctct gctggctgcc cttcttcatc 2460 gttaacattg tgcatgtgat ccaggataac ctcatccgta aggaagttta catcctccta 2520 aattggatag gctatgtcaa ttctggtttc aatcccctta tctactgccg gagcccagat 2580 ttcaggattg ccttccagga gcttctgtgc ctgcgcaggt cttctttgaa ggcctatggg 2640 aatggctact ccagcaacgg caacacaggg gagcagagtg gatatcacgt ggaacaggag 2700 aaagaaaata aactgctgtg tgaagacctc ccaggcacgg aagactttgt gggccatcaa 2760 ggtactgtgc ctagcgataa cattgattca caagggagga attgtagtac aaatgactca 2820 ctgctgtaaa gcagtttttc tacttttaaa gaccccccc cccccaacag aacactaaac 2880 agactattta acttgagggt aataaactta gaataaaatt gtaaaaattg tatagagata 2940 tgcagaagga agggcatcct tctgcctttt ttattttttt aagctgtaaa aagagagaaa 3000 aagtttatgt ctaaagagct ttagtcctag aggacctgag tctgctatat tttcatgact 3120 tttccatgta tctacctcac tattcaagta ttaggggtaa tatattgctg ctggtaattt 3180 gtatctgaag gagattttcc ttcctacacc cttggacttg aggattttga gtatctcgga 3240 cettteaget gtgaacatgg actetteece cacteetett atttgeteac acggggtatt 3300 ttaggcaggg atttgaggag cagcttcagt tgttttcccg agcaaaggtc taaagtttac 3360 agtaaataaa atgtttgacc atgccttcat tgcacctgtt tgtccaaaaac cccttgactg 3420 3451 gagtgctgtt gcctccccca ctggaaaccg c

<400> 7
cccgggttca agagattctc ctgtctcagc ctcccgagta gctgggacta caggtacgtg 60
ccaccacacc tggctaattt ttgtattttt agtagagaca agagttacac catattggcc 120
aggatctttt gctttctata gcttcaaaat gttcttaatg ttaagacatt cttaatactc 180
tgaaccatat gaatttgcca ttttggtaag tcacagacgc cagatggtgg caatttcaca 240
tggcacaacc cgaaagatta acaaactatc cagcagatga aaggattttt tttagtttca 300
ttgggtttac tgaagaaatt gtttgaattc tcattgcatc tccagttcaa cagataatga 360
gtgagtgatg ccacactctc aagagttaaa aacaaacaa caaaaaaatt aaaacaaaag 420
cacacaactt tctctctctg tcccaaaata catacttgca tacccccgct ccagataaaa 480
tccaaagggt aaaactgtct tcatgcctgc aaattcctaa ggagggcacc taaagtactt 540

gacagegagt gtgctgagga aateggeage tgttgaagte aceteetgtg etettgeeaa 600 gctcgggtga ggcaagttcg gagtacccag atggagacat ccgtgtctgt gtcgctctgg 720 atgectecaa gecagegtgt gtttacttte tgtgtgtgte accatgtett tgtgettetg 780 ggtgcttctg tgtttgtttc tggccgcgtt tctgtgttgg acaggggtga ctttgtgccg 840 gatggettet gtgtgagage gegegegagt gtgcatgteg gtgagetggg agggtgtgte 900 tcagtgtcta tggctgtggt tcggtataag tctgagcatg tctgccaggg tgtatttgtg 960 cctgtatgtg cgtgcctcgg tgggcactct cgtttccttc cgaatgtggg gcagtgccgg 1020 tgtgctgccc tctgccttga gacctcaagc cgcgcaggcg cccagggcag gcaggtagcg 1080 gccacagaag agccaaaagc tcccgggttg gctggtaagg acaccacctc cagctttagc 1140 cctctggggc cagccagggt agccgggaag cagtggtggc ccgcctcca gggagcagtt 1200 gggccccgcc cgggccagcc ccaggagaag gagggcgagg ggaggggagg gaaaggggag 1260 gagtgcctcg ccccttcgcg gctgccggcg tgccattggc cgaaagttcc cgtacgtcac 1320 ggcgagggca gttcccctaa agtcctgtgc acataacggg cagaacgcac tgcgaagcgg 1380 cttcttcaga gcacgggctg gaactggcag gcaccgcgag cccctagcac ccgacaagct 1440 gagtgtgcag gacgagtccc caccacacc acaccacagc cgctgaatga ggcttccagg 1500 cgtccgctcg cggcccgcag agccccgccg tgggtccgcc tgctgaggcg cccccagcca 1560 gtgcgcttac ctgccagact gcgcgccatg gggcaacccg ggaacggcag cgccttcttg 1620 ctggcaccca atggaagcca tgcgccggac cacgacgtca cgcagcaaag ggacgaggtg 1680 tgggtggtgg gcatgggcat cgtcatgtct ctcatcgtcc tggccatcgt gtttggcaat 1740 gtgctggtca tcacagccat tgccaagttc gagcgtctgc agacggtcac caactacttc 1800 atcacttcac tggcctgtgc tgatctggtc atgggcctgg cagtggtgcc ctttggggcc 1860 gcccatattc ttatgaaaat gtggactttt ggcaacttct ggtgcgagtt ttggacttcc 1920 attgatgtgc tgtgcgtcac ggccagcatt gagaccctgt gcgtgatcgc agtggatcgc 1980 tactttgcca ttacttcacc tttcaagtac cagagcctgc tgaccaagaa taaggcccgg 2040 gtgatcattc tgatggtgtg gattgtgtca ggccttacct ccttcttgcc cattcagatg 2100 cactggtacc gggccaccca ccaggaagcc atcaactgct atgccaatga gacctgctgt 2160 gacttettea egaaceaage etatgeeatt geetetteea tegtgteett etaegtteee 2220 ctggtgatca tggtcttcgt ctactccagg gtctttcagg aggccaaaag gcagctccag 2280 aagattgaca aatctgaggg ccgcttccat gtccagaacc ttagccaggt ggagcaggat 2340 gggcggacgg ggcatggact ccgcagatct tccaagttct gcttgaagga gcacaaagcc 2400 ctcaagacgt taggcatcat catgggcact ttcaccctct gctggctgcc cttcttcatc 2460 gttaacattg tgcatgtgat ccaggataac ctcatccgta aggaagttta catcctccta 2520 aattggatag gctatgtcaa ttctggtttc aatcccctta tctactgccg gagcccagat 2580 ttcaggattg ccttccagga gcttctgtgc ctgcgcaggt cttctttgaa ggcctatggg 2640 aatggctact ccagcaacgg caacacaggg gagcagagtg gatatcacgt ggaacaggag 2700 aaagaaaata aactgctgtg tgaagacctc ccaggcacgg aagactttgt gggccatcaa 2760 ggtactgtgc ctagcgataa cattgattca caagggagga attgtagtac aaatgactca 2820 ctgctgtaaa gcagtttttc tacttttaaa gaccccccc ccccaacag aacactaaac 2880 agactattta acttgagggt aataaactta gaataaaatt gtaaaaattg tatagagata 2940 tgcagaagga agggcatcct tctgcctttt ttattttttt aagctgtaaa aagagagaaa 3000 aagtttatgt ctaaagagct ttagtcctag aggacctgag tctgctatat tttcatgact 3120 tttccatgta tctacctcac tattcaagta ttaggggtaa tatattgctg ctggtaattt 3180 gtatctgaag gagattttcc ttcctacacc cttggacttg aggattttga gtatctcgga 3240 cettteaget gtgaacatgg actetteece cacteetett atttgeteac acggggtatt 3300 ttaggcaggg atttgaggag cagcttcagt tgttttcccg agcaaaggtc taaagtttac 3360 agtaaataaa atgtttgacc atgccttcat tgcacctgtt tgtccaaaac cccttgactg 3420